REMARKS

Upon entry of the present amendments, claims 1-8 and 11 are pending in the present application. Claims 1-5 and 11 have been amended to more clearly define the present invention. Claims 9, 10 and 12-20 have been canceled, without prejudice. Applicants reserve the right to pursue the subject matter of these claims in a later application. No new matter has been added by the present amendments.

SPECIFICATION

The Examiner has objected to the disclosure because the specification and the Raw Sequence Listing do not match with respect to SEQ ID NO:224 and has requested appropriate correction. Applicants have amended the specification (*i.e.* SEQ ID NOs: 224-225) to correctly correspond with the Raw Sequence Listing and therefore request withdrawal of the present objection.

SPECIES ELECTION

Applicants provisionally elected the nucleic acid sequence identified as SEQ ID NO:225, with traverse in Paper No. 10. As amended herein, the specification and claims now identifies elected nucleic acid sequence SEQ ID NO:225 as SEQ ID NO:224 to correspond with the Raw Sequence Listing. Applicants respectfully submit that the elected species is now identified as SEQ ID NO:224.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner has rejected claims 1-8 and 11 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action recites that the claims require an "ORX" nucleic acid or polypeptide, yet the specification does not define the term "ORX" such that one skilled in the art would know what is and what is not an "ORX" nucleic acid or polypeptide. Applicants traverse.

Applicants have amended claim 1 to specifically recite the ORX nucleic acid sequence comprising the nucleotide sequence of elected sequence SEQ ID NO:224. Applicants submit that SEQ ID NO:224 and complements thereof are defined in the specification (*see*, Specification at pg. 121, lines 1-45; pg. 232, lines 3-10) and therefore one skilled in the art would know what is defined by the ORX nucleic acid sequence comprising SEQ ID NO:224 and nucleic acid sequences complementary thereto.

Applicants submit that claim 1, as amended herein, and claims 2-8 and 11 which properly depend from claim 1, are not indefinite under 35 U.S.C. §112, second paragraph and therefore respectfully request withdrawal of the present rejection.

The Examiner has also rejected claims 2 and 9 (from which elected claim 11 depends) stating that the term "stringent conditions" is confusing because it is a relative term. Applicants traverse.

Applicants have cancelled claim 9 as drawn to a non-elected invention and have amended claim 11 to depend from claim 3. Applicants have amended claim 2 to recite that the nucleic acid molecule hybridizes under stringent hybridization conditions to a nucleic acid sequence complementary to an ORX nucleic acid molecule comprising SEQ ID NO:224. Applicants submit that the term "stringent hybridization conditions" is defined in the specification (*see*, Specification at pg. 236, line 7 - pg. 237, line 27) and that an example of "stringent hybridization conditions" is also defined (see, Specification at pg. 236, lines 25-29).

As such, Applicants submit that any person skilled in the art would be able to make and use the invention commensurate in scope with the claim 2, as amended herein, and therefore request withdrawal of the present rejection.

The Examiner has also rejected claim 2 for reciting "or the complement of said nucleic acid molecule" because there appears to be more than one "nucleic acid molecule" recited in claim 2. Applicants traverse.

Applicants have amended claim 2 to recite "...to a nucleic acid sequence complementary to an ORX nucleic acid molecule comprising SEQ ID NO:224 or a complement thereof" to more clearly define the present invention.

Therefore, Applicants submit that claim 2, as amended herein, is not indefinite under 35 U.S.C. §112, second paragraph and therefore respectfully request withdrawal of the present rejection.

The Examiner has also rejected claim 3 for reciting "conservative substitutions" stating that the term "conservative substitution" is used in the art as a relative term. Applicants traverse.

Applicants have amended claim 3 to recite "...polypeptide comprising one or more conservative amino acid substitutions." Applicants submit that the term "conservative amino acid substitution" is defined in the specification (see, Specification at pg. 238, line 29 - pg. 239, line 12).

As such, Applicants submit that any person skilled in the art would be able to make and use the invention commensurate in scope with the claim 3, as amended herein, and therefore request withdrawal of the present rejection.

The Examiner has also rejected claim 9 (from which elected claim 11 depends) for failing to define the terms "derivative", "analogue" and "homolog".

Applicants have cancelled claim 9 as drawn to a non-elected invention and have amended claim 11 to depend from claim 3 and therefore request withdrawal of the present rejection.

REJECTIONS UNDER 35 U.S.C. § 101

Claims 1-8 and 11 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. It is the Examiner's position that the asserted specific utilities for the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed nucleic acids. Applicants traverse.

Pending claims 1-8, and 11, as amended herein, are directed to nucleic acid molecules comprising SEQ ID NO:224, complements thereof, polypeptides encoded thereby, and compositions and methods containing such nucleic acid or polypeptide molecules. The specification discloses that SEQ ID NO:224 is a novel member of the olfactory receptor (ORX) family and has conserved sequences shared by ORX family members and asserts a utility based, in part, on homology between SEQ ID NO:224 and known ORX family members (*See* specification pg. 222, line 33 to pg. 228 line 15).

The Utility Examination Guidelines state that "when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific

reasoning to rebut such an assertion." (Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1096). If the Examiner has sufficient evidence to rebut such an assertion, and rejects the claims for lack of utility, then the burden shifts back to the Applicant to provide evidence supporting such a well-established utility.

In this case, SEQ ID NO:224 contains the characteristic features of ORX family members including both a ORX ligand binding domain, and a heptahelical transmembrane domain within its overall sequence. (*See,* Specification at page 223 line 13 - line 20). Thus, the presence of these domains within the overall sequence of SEQ ID NO:224 demonstrates that SEQ ID NO:224 is a novel member of the ORX family. Accordingly, one skilled in the art would recognize that the disclosed sequence of the polypeptide of the present invention, which contains these consensus domains, can be expected to function as a member of the ORX family.

The ORX family is involved in discriminating between odor molecules and in cellular differentiation and cellular proliferation. Thus, SEQ ID NO:224 could be used in diagnosing, preventing and treating various diseases and disorders attributed to altered or aberrant function of ORX family members including, but not limited to, neurodegenerative, cell proliferative, angiogenic, hematopoietic, immunological, inflammatory, and tumor-related disorders and/or pathologies as disclosed throughout the specification (*e.g., See*, specification at pg. 289, lines 20-26). Therefore, Applicants assert that the polypeptide of SEQ ID NO:224, as a novel member of this family, has an art recognized specific, substantial, and credible utility.

Moreover, nucleic acid and amino acid homology is commonly determined by the skilled artisan using BLAST (*e.g.,* BLASTX, BLASTN, BLASTP, etc.). Here, the nucleotide sequence of SEQ ID NO: 224 is highly homologous to members of the ORX family from various species (*e.g., Homo sapiens*, *Pan troglodytes*, Mus musculus, *Rattus norvegicus*, etc.) as determined by BLASTN analysis including, but not limited to, (gi|7211484|gb|AF179735.1|AF179735; gi|7211473|gb|AF179729.1|AF179729; gi|21928224|dbj|AB065456.1|; gi|20893120|ref|XM_156335.1|; gi|18479485|gb|AY073094.1|; gi|27669284|ref|XM_221575.1|).

The Utility Examination Guidelines further state that "when a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein." (Fed. Reg., Vol. 66. No. 4, January 5, 2001, p. 1096). ORX protein family members share a specific, substantial, and

credible utility and are sufficiently conserved, thereby imputing the same utility to a novel member of their protein class, such as proteins encoded by SEQ ID NO:224.

The foregoing demonstrates that nucleic acid molecules comprising SEQ ID NO:224, complements thereof, and polypeptides encoded thereby of the present invention have utility as a homologous, functional member of the ORX family. Accordingly, Applicants request that this rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-18 and 11 are rejected under 35 U.S.C. § 112, first paragraph for alleging that since the invention is not supported by either a specific or substantial asserted utility, one skilled in the art would not know how to use the claimed invention. Applicants traverse.

For the reasons set forth above, Applicants submit that the claimed invention has a specific and substantial or well-established utility. Therefore, this rejection is now moot and should be withdrawn.

Claims 1-18 and 11 are also rejected under 35 U.S.C. § 112, first paragraph for alleging that Applicants have not provided sufficient guidance as to how to make and use polynucleotides or polypeptides which are not 100% identical to those disclosed. Applicants traverse.

Applicants have amended claim 1 to specifically recite the ORX nucleic acid sequence comprising the nucleotide sequence of elected sequence SEQ ID NO:224. Applicants submit that SEQ ID NO:224, complements thereof and polypeptides encoded thereby are defined in the specification (*see*, Specification at pg. 121, lines 1-45; pg. 232, lines 3-10) to enable any person skilled in the art to make and use the present invention as claimed.

Applicants submit that claim 1, as amended herein, and claims 2-8 and 11 which properly depend from claim 1, meet the written description and enablement provisions under 35 U.S.C. §112, first paragraph and therefore respectfully request withdrawal of the present rejection.

REJECTIONS UNDER 35 U.S.C. § 102 AND 35 U.S.C. § 103

Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Freitag et al., Neuron, 15(1383-1392) 1995 ("Freitag"). The Examiner states that Freitag teaches the amplification of genomic DNA using primers

OR3.1-OR7.1 and therefore the claimed polynucleotides are not patentably distinct from those disclosed by Freitag. Applicants traverse.

Applicants have amended claim 1 to recite the nucleic acid molecule of SEQ ID NO:224 or a complement thereof. Freitag teaches the use of DNA from *Xenopus laevis* to amplify olfactory receptor (OR) related genes using PCR. Freitag does not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a compliment thereof or a polypeptide encoded thereby.

Thus, Freitag does not teach or suggest the limitations of the claimed invention. Accordingly, Applicants assert that claim 1, as amended herein, and claims 2-8 and 11, which depend from claim 1, are patentably distinct from the polynucleotides of Freitag. Therefore, this rejection of these claims should be withdrawn.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ben-Arie et al., Human Molecular Genetics 3(2)229-235, 1994 ("Ben-Arie"). The Examiner states that the claimed polynucleotides are not patentably distinct from those disclosed by Ben-Arie. Applicants traverse.

Applicants have amended claim 1 to recite the nucleic acid molecule of SEQ ID NO:224 or a complement thereof. Ben-Arie teaches the cloning of 16 human olfactory receptor (OR) genes and the great sequence variability between those OR genes. Ben-Arie does not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a compliment thereof or a polypeptide encoded thereby. Moreover, Applicants submit that Ben-Arie teaches away from the nucleic acid molecule of SEQ ID NO:224 or a complement thereof or a polypeptide encoded thereby when it teaches that the cloned OR sequences display as much sequence variability as any randomly selected group of ORs.

Thus, Ben-Arie does not teach or suggest the limitations of the claimed invention. Accordingly, Applicants assert that claim 1, as amended herein, and claims 2-8 and 11, which depend from claim 1, are patentably distinct from the polynucleotides of Ben-Arie. Therefore, this rejection of these claims should be withdrawn.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freitag or Ben-Arie, in view of Kiefer et al., Biochemistry 1996, 35:16077-16084 ("Kiefer"). The Examiner states that the encoded receptor polypeptides taught by either Freitag or Ben-Arie could be produced using the method taught by Kiefer. Applicants traverse.

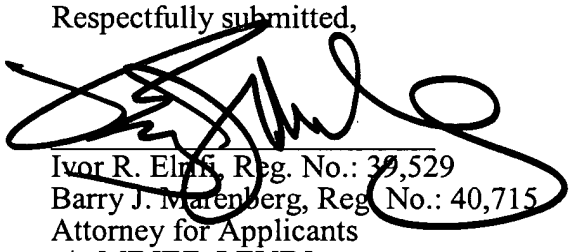
Applicants have amended claim 11 to indirectly depend from claim 1 and have amended claim 1 to recite the nucleic acid molecule of SEQ ID NO:224 or a complement thereof. Kiefer teaches the expression and purification of an olfactory receptor (OR5). As discussed *supra*, Freitag or Ben-Arie do not teach or suggest the human nucleic acid sequence of SEQ ID NO:224, a compliment thereof or a polypeptide encoded thereby. Applicants contend that, while Kiefer teaches the expression of an olfactory receptor, Kiefer alone or in combination with the teachings of Freitag or Ben-Arie, does not teach or suggest expression of the human nucleic acid sequence of SEQ ID NO:224 or its compliment.

Thus, Freitag or Ben-Arie in view of Kiefer do not teach or suggest all the limitations of the claimed invention. Accordingly, Applicants assert that claim 11, as amended herein, which depends from amended claim 1, is not anticipated by Freitag or Ben-Arie in view of Kiefer. Therefore, this rejection of these claims should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Dated: February 27, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph beginning on line 31 at page 121 has been replaced with the following:

/translation="VAICNPLLYPVMMSNKLSAQLLSISYVIGFLHPLVHVSLLLRLTFCRFNIIHY
FYCEILQLFKISCNGPSINALIIFIFGAFIQIPTLMTIIISYTRVLFDILKKKSEKGRSKAFSTC
GAHLLSVSLYYGTLIFMYVRPASGLAEDQDKVYSLFYTIIIPLL" (SEQ ID NO:225 [224]).

The paragraph beginning on line 37 at page 121 has been replaced with the following:

1 tgtagccata tgtaatccct tgctttatcc agtgatgatg tccaacaaac tcagcgctca
61 gttgctaagt atttcatatg taattggttt cctgcatcct ctggttcatg tgagtttact
121 attgcgacta actttctgca ggtttaacat aatacattat ttctactgtg aaattttaca
181 actgttcaaa atttcatgca atggtccatc tattaacgca ctaataatat ttatttttgg
241 tgcttttata caaataccca ctttaatgac tatcataatc tcttatactc gtgtgctctt
301 tgatattctg aaaaaaaagt ctgaaaaggg cagaagcaaa gccttctcca catgcggcgc
361 ccatctgctt tctgtctcat tgtactacgg aactctgatc ttcatgtatg tgcgtcctgc
421 atctggctta gctgaagacc aagacaaagt gtattctctg ttttacacga ttataattcc
481 cctgcta (SEQ ID NO:224 [225]).

In the Claims:

Claims 1, 2, 4, 5 and 11 have been amended as follows:

1. (Amended) An isolated nucleic acid molecule encoding an olfactory receptor (ORX) polypeptide, wherein said molecule comprises a nucleotide sequence [that is at least 95% identical to an ORX nucleic acid sequence] of SEQ ID NO:224, or a [the] complement thereof [of said nucleic acid molecule].

2. (Amended) The nucleic acid molecule of claim 1, wherein said molecule hybridizes under stringent hybridization conditions to a nucleic acid sequence complementary to an ORX nucleic acid molecule comprising SEQ ID NO:224, or a [the] complement thereof [of said nucleic acid molecule].

3. (Amended) The nucleic acid molecule of claim 1, wherein said molecule encodes an ORX polypeptide [or an amino acid sequence] comprising one or more conservative amino acid substitutions [in the amino acid sequence of an ORX polypeptide].

4. (Amended) The nucleic acid molecule of claim 1, wherein said molecule encodes an ORX polypeptide, or a [the] complement thereof [of said nucleic acid molecule].

5. (Amended) An oligonucleotide of less than 100 nucleotides in length, which comprises at least 6 contiguous nucleotides of the [an] ORX nucleic acid molecule of claim 1, or a complement thereof.

11. (Amended) A method of producing the polypeptide of claim 3 [9], said method comprising the step of culturing a host cell under conditions in which the nucleic acid molecule is expressed.